

**REMARKS**

Applicants submit that claims 45-59 and 68-80 have been canceled without prejudice, and Applicants further reserve the right to prosecute said canceled claims in a continuation or divisional application. Attached herewith, pursuant to 37 C.F.R. § 1.173(c), is a chart, at Appendix A, providing the status of all claims. Further included in the chart, pursuant to 37 C.F.R. § 1.173(c), is an indication of the passages in the originally filed application where, at the very least, the claims find support. In addition, a clean set of all pending claims, original and added, are provided for the convenience of the Examiner at Appendix B.

An explanation of the above amendments to claims 15, 60, 65, 81, and 86 is as follows:

Claim 15 was amended to remove the language "for example,...".

Claim 60 was amended to include the elements recited in canceled claims 49 and 45 from which claim 60 depended in order to allow claim 60 to be written in independent form.

Claim 65 was amended to include the elements recited in canceled claims 49 and 45 from which claim 65 depended in order to allow claim 65 to be written in independent form.

Claim 81 was amended to include the elements recited in canceled claim 70 from which claim 81 depended in order to allow claim 81 to be written in independent form.

Claim 86 was amended to include the elements recited in canceled claim 70 from which claim 86 depended in order to allow claim 86 to be written in independent form.

It is respectfully submitted that entry of the amendments submitted herewith introduce no new matter to the reissue application.

**OBJECTION UNDER 37 C.F.R. § 1.75**

The Office objected to claims 45-48 under 37 C.F.R. § 1.75 as being a substantial duplicate of claims 6-8. Claims 45-48 have been canceled by amendment, thus obviating the above rejection.

**FIRST REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH**

The Office rejected claims 49-91 under 35 U.S.C. § 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. The Office further stated that evidence that claim 49, 70, 81, and 88 fail(s) to correspond in scope with that which applicant(s) regard as the invention can be found in Remarks filed in parent application

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SN 08/823,461, filed December 29, 1999. The Office stated that in that paper, applicant stated at page 5 thereof that the invention is for the treatment of pain with olanzapine, an anti-psychotic agent not known to be useful for the treatment of pain. The Office then further stated that this statement indicates that the invention is different from what is defined in the present claims(s) because claims 49-91 are now drawn to olanzapine and anti-psychotic drugs such as tricyclic antidepressants which are not known to be anti-pain drugs.

Applicants respectfully submit that in view of the above amendments, pending claims 60-67 and 81-91 relate to pharmaceutical compositions and pharmaceutical compositions in unit dose form, and more specifically, to combinations of olanzapine and serotonin reuptake inhibitors and combinations of olanzapine and mixed serotonin-norepinephrine reuptake inhibitors, rather than tricyclic antidepressants. In addition, Applicants submit that the specification defines "Drug Useful in the Treatment of Pain" at column 5, lines 4-25 as including serotonin reuptake inhibitors and mixed serotonin-norepinephrine reuptake inhibitors. Thus, Applicants respectfully assert that serotonin reuptake inhibitors and mixed serotonin-norepinephrine reuptake inhibitors fall within the specification definition of "Drug Useful in the Treatment of Pain". Moreover, Applicants respectfully assert that nowhere on page 5 in the Remarks filed in parent application SN 08/823,461, filed December 29, 1999, do Applicants state that the invention is only for the treatment of pain with olanzapine.

In view of the above, it is respectfully asserted that Applicants intended pharmaceutical composition claims 60-67 and pharmaceutical composition in unit dose form claims 81-91 to be part of their invention. Thus, Applicants respectfully submit that rejection of claims 60-67 and 81-91 under 35 U.S.C. § 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention is improper.

#### SECOND REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

The Office rejected claims 49, 70, 81, and 86 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants respectfully submit that claims 49 and 70, which contained the parenthetical "for example" language therein, have been canceled. Although claims 81 and 86 depended ultimately on claim 70, they do not contain the parenthetical "for example"

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language after the amendments entered herewith. Therefore, Applicants submit that rejection of claims 49, 70, 81, and 86 under 35 U.S.C. § 112, second paragraph, has been obviated.

**REJECTION UNDER 35 U.S.C. § 103(a)**

The Office rejected claims 49-91 under 35 U.S.C. § 103(a) as being unpatentable over applicant's admissions and the Merck Index reference. The Office asserted that Applicants admitted that their invention related to the use of olanzapine, an antipsychotic agent, to treat pain not previously known. In addition, the Office submitted that Merck teaches at page 2421 that clozapine is a tricyclic antipsychotic agent.

Whether pending claims 60-67 and 81-91 are unpatentable under 35 U.S.C. § 103(a) over Applicant's admissions and the Merck Index depends upon whether the differences between the subject matter sought to be patented and the prior art, as a whole, would have been obvious at the time the invention was made to a person having ordinary skill in the art to which the subject matter pertains. Changes from the prior art must be evaluated in terms of the whole invention, including whether the prior art provides any teaching or suggestion to one of ordinary skill in the art to make the changes that would produce the claimed invention.

The statement made by Applicants on page 5 in the Remarks filed in parent application SN 08/823,461, filed December 29, 1999, which the Office appears to be referring to, was as follows:

"Olanzapine was known to be an antipsychotic agent; it was not known to be useful for the treatment of pain"

Applicants respectfully assert that the above statement is not an admission that their invention simply related to the use of olanzapine, an antipsychotic agent, to treat pain not previously known. Rather, this statement was a fact that was relevant to the rejection made by the Office wherein In re Kerkhoven was cited for the proposition that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose. Thus, in response to In re Kerkhoven, Applicants further stated on page 5 in the Remarks filed in parent application SN 08/823,461, filed December 29, 1999, the following:

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“Applicants, on the other hand, are claiming a combination of two compositions, one of which is taught by the prior art to be useful for an entirely different purpose.”  
(emphasis added)

Applicants respectfully assert, that in view of the above statement, when read in light of the claims and the specification, the present invention is not simply related to the use of olanzapine *per se* to treat pain, rather, the present invention is related to treating pain with the combination of olanzapine and a Drug Useful for Treating Pain, as defined in the specification, and also to pharmaceutical compositions thereof.

In addition, Applicants respectfully submit that nowhere does the present application teach the combination of clozapine with olanzapine for treating pain. Moreover, claims 60-67 and 81-91 are directed to combinations of olanzapine with a serotonin reuptake inhibitor, such as fluoxetine, or the combination of olanzapine with a serotonin-norepinephrine reuptake inhibitor, such as duloxetine. Applicants respectfully assert that clozapine does not fall within the class of either serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors.

In view of the above, Applicants respectfully assert that neither the Applicants statement on page 5 in the Remarks filed in parent application SN 08/823,461, filed December 29, 1999, nor the Merck Index relating to the definition of clozapine, suggests much less teaches the pharmaceutical compositions of claims 60-67 and 81-91 to one of ordinary skill in the art. Thus, one of ordinary skill in the art would not be motivated to make the changes necessary to the prior art so as to arrive at the pharmaceutical compositions of the present invention. Therefore, Applicants respectfully assert that rejection of claims 60-67 and 81-91 under 35 U.S.C. § 103(a) as being unpatentable over applicant's admissions and the Merck Index reference is improper.

#### **REJECTION ON PAGE 5, SECOND PARAGRAPH OF OFFICE ACTION**

The Office asserted that there is a lack of teaching in the specification that the claimed active agents as claimed in claims 49-91 are also known to treat pain, and that, the claimed compounds in claims 49-91 are not within the scope of applicants' definition of pain as set forth at column 6, lines 57-67.

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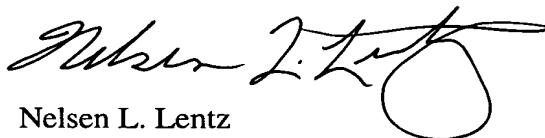
Applicants respectfully submit that the specification defines "Drugs Useful in the Treatment of Pain" in column 5. In particular, column 5, lines 11-23 unambiguously states:

"Drugs Useful in the Treatment of Pain shall also encompass classical analgesic agents known to the artisan. See for example, Goodman and Gillman, The Pharmacological Basis of Therapeutics, 5<sup>th</sup> edition, Macmillan Publishing Co., 1975, pp 325-358, and similar references commonly consulted by the skilled artisan. Thus, the term shall include, for example, ... serotonin reuptake inhibitors (for example, fluoxetine, paroxetine, citalopram, sertraline), mixed serotonin-norepinephrine reuptake inhibitors (for example venlafaxine duloxetine)..." (emphasis added).

In view of the above, Applicants respectfully assert that the compounds claimed in pending claims 60-67 and 81-91 are clearly defined and set forth in the specification under the broad term "Drugs Useful in the Treatment of Pain". Therefore, Applicants assert that rejection of claims 60-67 and 81-91 for lack of teaching in the specification is improper.

In view of the above amendments and remarks, Applicants submit that claims 60-67 and 81-91 are in condition for allowance. Reconsideration and withdrawal of the rejections is respectfully requested and allowance of claims 1-44, 60-67, and 81-91 is kindly solicited.

Respectfully submitted,



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